REMARKS

Claims 1 and 19 have been amended to correct informalities or to delete subject matter not necessary to claim the invention. No new matter has been added.

Rejection under 35 USC § 112, first paragraph

Claims 1, 3-19, 21 are rejected for lack of written description. The rejection is traversed.

The Examiner states that the recitations "a first identification step" and "a second identification step" are not supported in the specification. Claim 1 and claim 19, from which the remaining claims subject to the rejection depend, have been amended to remove reference to this subject matter. Accordingly, the rejection can be withdrawn.

Rejection under 35 USC § 112, second paragraph

Claims 1, 3-19, 21 are rejected as indefinite. The rejection is traversed.

The Examiner states that the recitations "a first identification step" and "a second identification step" are indefinite. Claim 1 and claim 19, from which the remaining claims subject to the rejection depend, have been amended to remove reference to the disputed subject matter. Accordingly, the rejection can be withdrawn.

Rejections under 35 USC § 102

Claims 1, 3-6, 10, 13-16, 18, and 21 are rejected as anticipated under 35 USC § 102(b) by Whitcombe et al., WO97/42345 ("Whitcombe"). The rejection is traversed.

The method specified in claim 1, from which the remaining claims depend, requires removing a complex that includes at least one nucleic acid sequence of interest from a population

of nucleic acids (last recited step). This nucleic acid sequence of interest is present throughout the recited steps, i.e., it is present - from the outset - in the provided population of nucleic acid molecules (see first recited step), as well as during the subsequent contacting, attaching, and immobilizing steps.

In contrast, the method described in Whitcombe does not result in the isolation and detection of the actual nucleic acid sequence of interest itself from a starting population of nucleic acid molecules. Instead, Whitcombe describes a method in which a series of extension products are prepared. The first extension product is generated from a diagnostic primer that includes a tail sequence with a tag region and a detector region (see page 1, line 28-page 2, line 4). The extension product then acts as a template for the extension of a further primer that hybridizes to a locus at a distance from the diagnostic base sequence; the further primer when extended forms a further extension product (page 2, lines 5-10; see also claim 1). The presence or absence of a diagnostic base sequence is detected by reference to a detector region in the further extension product using methods discussed at page 2, line 11, to page 3, line 6 and claims 2-6.

Thus, Whitcombe describes a method that detects not the starting nucleic acid sequence itself but instead an amplification product whose synthesis is dependent on the presence of a sequence of interest. Therefore, this reference does not describe the invention of claims 1, 3-6, 10, 13-16, 18, and 21.

Claims 1, 3-15, 17, 18, and 21 are rejected as anticipated under 35 USC § 102 (e) by Lundeberg et al., US Patent No. 6, 482,592 ("Lundeberg"). The rejection is traversed.

Claim 1, from which the remaining claims subject to the rejection depend, requires that attachment of the separation group is conditional on the presence of a distinguishing element in

the vicinity of the bound targeting element. Lundeberg does not describe a method in which attachment of a separation group is conditional upon a distinguishing element being in the vicinity of the already bound targeting element.

The Examiner states that the modular oligonucleotides described in Lundeberg corresponds to a targeting element, and that a modulating module/capture probe corresponds to a separation group (page 8, second paragraph of the Office Action). The modular oligonucleotide and modulating module/capture probe are oligonucleotides that bind to their respective complementary target sequences. While Lundeberg teaches that binding of one oligonucleotide may be enhanced by the presence of a second oligonucleotide in the vicinity of the first oligonucleotide, the binding of the first oligonucleotide is not conditional upon a distinguishing element being in the vicinity of a bound targeting element. That is, a modulating module / capture probe will bind to a complementary target sequence even in the absence of a second oligonucleotide, and regardless of the distance between the oligonucleotides. See, for example, col. 1, lines 57-63, where Lundeberg states (emphasis added):

> Surprisingly, is has now been found that modular probes or primers composed of at least two modules (oligonucleotides) which bind to adjacent regions of target DNA exhibit improved binding relative to a single oligonucleotide spanning the same length as the separate modules (see WO98/13522). For example, it has been found that two adjacent 18-mer oligonucleotides bind more efficiently to target DNA than the composite 36-mer oligonucleotide.

However, specific binding of shorter capture probes to target nucleic acids does occur, even in the absence of modular probes (see, for example, page 16, line 21 to page 19, line 4 of Whitcombe, which discloses the use of an 18 nucleotide primer (HpH1F) and a 20 nucleotide primer (HpH1R) to amplify genomic DNA).

What Lundeberg does not teach is that binding of one oligonucleotide is conditional on the binding of a second modular probe already bound in the vicinity of the first oligonucleotide. Thus, Lundeberg does not describe the feature of Applicant's invention requiring that attachment of the separation group be conditional on the presence of a distinguishing element in the vicinity of a bound targeting element. Therefore, it does not anticipate claim 1, nor the claims depending from the rejection.

In view of the foregoing comments, Applicants respectfully request reconsideration and withdrawal of the rejections for anticipation.

Rejections under 35 USC § 103(a)

Claim 16 is rejected as unpatentable over Lundeberg in view of Whitcombe. The rejection is traversed.

Claim 16 depends from claim 1 and further requires that the distinguishing element is a single nucleotide polymorphism. As is explained above, Lundeberg does not make obvious the invention of claim 1 because it discloses oligonucleotides as targeting elements and separation groups. Binding of the oligonucleotides is not conditional, but instead is, according to Lundeberg, enhanced when both oligonucleotides are present. Lundeberg neither discloses nor suggests any separation groups that bind conditionally on the presence of a distinguishing element and a bound targeting element in its vicinity.

Whitcombe is used to complete the rejection by teaching the identification of single nucleotide polymorphisms. However, it, fails to disclose or suggests a separation group that binds conditionally on the presence of a distinguishing element and a bound targeting element in the vicinity nucleic of a acid sequence of interest, and wherein the nucleic acid sequence of

interest is present in a provided population of nucleic acid molecules (see first recited step), as well as during the subsequent contacting, attaching, and immobilizing steps. Thus, claim 1 is non-obvious over the combination of Lundeberg and Whitcombe. Because claim 16 depends from claim 1, it too, is non-obvious over the combination of Lundeberg and Whitcomb. Therefore, the cited references do not render claim 16 prima facie obvious.

Claim 19 has been rejected as obvious over Lundeberg. The rejection is traversed. Claim 19 is drawn to a method in which removal of the separation group is conditional on the absence of the distinguishing element in the vicinity of the bound targeting element. There is no suggestion in Lundeberg of a method with this step. Therefore, claim 19 is not *prima facie* obvious over this reference.

Applicants respectfully request reconsideration and withdrawal of the rejections for obviousness.

The Commissioner is hereby authorized to charge payment of any fees required in connection with the papers transmitted herewith, or credit any overpayment of same, to Deposit Account No. 50-0311 (Reference No. 22650-001CIP).

Respectfully submitted,

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